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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/041,236	03/11/98	LUO	Y EX98-001

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EXAMINER	
LEE, L	
ART UNIT	**PAPER NUMBER**
1645	6

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Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No. 09/041,236	Applicant(s) Luo
	Examiner Li Lee	Group Art Unit 1645

☐ Responsive to communication(s) filed on _____ .

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) *1-9* is/are pending in the application.

Of the above, claim(s) *3-9* is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *1 and 2* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☒ Claims *1-9* are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐approved ☐disapproved.

☐ The specification is objected to by the Examiner.

☒ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____ .

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____ .

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☐ Notice of References Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

Election/Restriction

1. Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claims 1 and 2, drawn to isolated polypeptide, classified in class 530, subclass 350.

II. Claims 3-6, drawn to a nucleic acid and expression system, classified in class 530, subclass 23.1.

III. Claim 7, drawn to a method for modulation a cellular physiology by using a polypeptide, classified in class 514, subclass 12.

IV. Claims 8 and 9, drawn to a method for modulation a cellular physiology by using a nucleic acid, classified in class 514, subclass 44.

2. The inventions are distinct, each from the other because of the following reasons:

Groups I and II are drawn to different products. The claims of Group I are drawn to a polypeptide, those of Group II are drawn to a polynucleotide. The inventions can be shown to be distinct because they are made by different methods (e.g., recombinant production, in vitro chemical synthesis) and because they are physically (e.g., nucleic acids, amino acids) and functionally distinct chemical entities (e.g., mediate biological activity, encode proteins). Thus, the product is distinct from each other.

3. Inventions of Group I and Group III are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the

process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case, the polypeptide product of Group I can be used materially different such as making antibodies or in assays for the identification of agonists or antagonist of the receptor protein other than modulating a cellular physiology.

4. Inventions Group II and Group IV are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case the nucleic acid product of Group II can be used materially different such as producing recombinant protein or nucleic acid hybridization assay other than modulating a cellular physiology.

Inventions Group I and Group IV are distinct because the product of polypeptide is not required in the Group IV invention. The polypeptide can neither be utilized nor made by the method of invention IV.

Inventions Group II and Group III are distinct because the product of polynucleotide of Group II is not required in the Group III invention. The polynucleotide can neither be utilized nor made by the method of invention III.

5. Because these inventions are distinct for the reasons given above and have acquired a separate status in the art because of their recognized divergent subject matter, restriction for examination purposes as indicated is proper.

6. During a telephone conversation with Richard Osman on 3/26/99 a provisional election was made with traverse to prosecute the invention of group I, claims 1 and 2. Affirmation of this election must be made by applicant in replying to this Office action. Claims 3-9 withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

7. Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a petition under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(I).

Oath/Declaration

8. The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02.

The oath or declaration is defective because:

Both inventors original signatures are lacking.

Claim Objections

9. Claim 2 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form.

Claim 2 is objected as it broadens up the limitation of claim 1 of full length SEQ ID NO:2 by reciting "immunogenicity" which indicates minim 6 residues in length in order to elicit a B cell immune response. .

Claim Rejections - 35 USC § 112

10. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

11. Claims 1 and 2 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a polypeptide selected from the group consisting of (a), (b), © and (d) of SEQ ID NO:2, having the activities of claim 2 does not reasonably provide enablement for multi/shuffled domains polypeptide of SEQ ID NO:2. The specification does not

enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use and make the invention commensurate in scope with these claims.

The claims 1 and 2 recite an isolated polypeptide comprising at least one of (a) SEQ ID NO:2, (b) at least 100 contiguous residues of SEQ ID NO:2, © at least 60 contiguous residues of SEQ ID NO:2, and (d) at least 12 contiguous residues of SEQ ID NO:2. This encompasses an single polypeptide molecule with covalent multi domains (or shuffled domains) of amino acid residues having a sequence of (a), (b), or © and (d). The written description is limited to polypeptide SEQ ID NO:2. The specification lacks any description of how to use any multi/shuffled domain SEQ ID NO:2 polypeptide which act as an sema K1 as instantly claimed. The claim is not enabled for using any multi domains of SEQ ID NO:2 polypeptide, because the following reasons: 1) the specification lacks any written description of any method which use the multi domains of SEQ ID NO:2 polypeptide, 2) the specification fails to teach what the biological function of a multi domains of SEQ ID NO:2 polypeptide is, 3) the specification fails to teach what are the critical protein residues that can be shuffled and still achieve an sema K1 protein. As to points 1)-3), the specification fails to provide a written description of using any multi domains of SEQ ID NO:2 polypeptide which function as an sema K1. The specification fails to teach the critical advantage of using such a polypeptide involved in the function of the multi domains of SEQ ID NO:2 polypeptide, such that the skilled artisan even begin to test, use or make a multi domains of SEQ ID NO:2 polypeptide. The specification fails to teach the actual biological function of multi domains of SEQ ID NO:2 polypeptide. One skilled in the art would have reason

to doubt alleged function of the protein because the specification fails to teach that the multi domains of SEQ ID NO:2 polypeptide actually function as asserted and the art teaches that genetically recombinant multi domains polypeptide can decrease or increase it's native biological functions. Even if one were to demonstrate that multi domains of SEQ ID NO:2 polypeptide functioned as an sema K1, the specification is not enabled for multi domains of SEQ ID NO:2 polypeptide because the specification fails teach even one method which one skilled in the art could be able to use it with activity. No assay for multi domains of SEQ ID NO:2 polypeptide is set forth in the specification which could allow one skilled in the art to screen for functionally equivalent multi domains of SEQ ID NO:2 polypeptide and the specification does not specifically point out to a particular one in the art could be relied upon for screening. One of skill in the art would be reduced to merely randomly shuffle SEQ ID NO:2 and claimed residues in SEQ ID NO:2 which would lead to unpredictable results regarding the functional activity of the multi domains of SEQ ID NO:2 polypeptide. Moreover, protein chemistry is probably one of the most unpredictable areas of biotechnology and the art teaches that the significance of any particular amino acid and sequences for different aspects of biological activity can not be predicted a *priori* and must be determined empirically on a case by case basis (Rudinger et al., in "Peptide Hormones", edited by Parsons, J.A., University Park Press, June 1976, page 6). The art specifically teaches that even a single amino acid change in a protein leads to unpredictable change in the biological activity of the protein. For example, replacement of a single lysine residue at position 118 of the acidic fibroblast growth factor by glutamic acid led to a substantial loss of

heparin binding, receptor binding, and biological activity of the protein (Burgess et al., The Journal of Cell Biology, 111:2129-2138, 1990). In transforming growth factor alpha, replacement of aspartic acid at position 47 with alanine, or asparagine did not affect biological activity while replacement with serine or glutamic acid sharply reduced the biologic activity of the mitogen (Lazar et al., Molecular and Cellular Biology, 8(3):1247-1252, 1988). These reference demonstrate that even a single amino acid substitution or what appears to be an inconsequential chemical modification will often dramatically affect the biological activity of a protein. Similarly, the domain shuffling can dramatically alter the folding of a protein. The biological function of such shuffled domain proteins are unpredictable due to unpredictable biological activity of proteins misfolding. The specification has not conceived how to use any other functionally equivalent multi domains of SEQ ID NO:2 polypeptide. Since, the specification lacks a written description of any multi domains of SEQ ID NO:2 polypeptide, it is not enabled for this language because it fails to enable the skilled artisan to envision how to use the multi domains of SEQ ID NO:2 polypeptide, as well as the detailed chemical structure of the claimed multi domains of SEQ ID NO:2 polypeptide, as well as the screening method of obtaining them, one of skilled in the art would be unable to use the multi domains of SEQ ID NO:2 polypeptide encompassed by the instant claims.

In view of the lack of written description of any multi/shuffled domains of SEQ ID NO:2 polypeptide that functions equivalently to the protein of SEQ ID NO:2, the lack of enabling description of any potential means of using and making multi/shuffled domains of SEQ ID NO:2

polypeptide, the unpredictability associated with using and making multi/shuffled domains of SEQ ID NO:2 polypeptide encompassed in the scope of the claim as set forth above, the lack of teaching even a beginning point for multi domains of SEQ ID NO:2 polypeptide for routine experimentation, the lack of an method to use multi domains of SEQ ID NO:2 polypeptide, lack of working examples commensurate in scope with the instant claims, the skilled artisan would be forced into undue experimentation to practice (i.e. use or make) the invention as is broadly claimed.

The claim 2 recites an isolated polypeptide having a binding inhibitory activity. However, the specification lacks any written description of any assay which could be used to determine for binding inhibitory activity. The specification fails to teach what this is, without such information one skilled in the art could not even begin to detect this activity, using conventional technology. One skilled in the art would have reason to doubt the alleged function of the protein because the specification fails to teach that the protein actually function as asserted. Applicant has not provided any guidance nor specific characteristics to the claimed protein binding inhibitory activities which would lead one of skill in the art to predict a binding inhibitory activity. One skilled in the art would have to independently develop many assays to test for the binding inhibitory activity of the protein in order to screen for many known possible protein binding inhibitory activities. One of skill in the art could not use conventional binding assay because one would not know what activity to screen for (binding/ or signaltransduction?). The specification provides no guidance as to the certain issue and therefor, one skilled in the art would be required

to perform undue experimentation to identify such. Therefor, one skilled in the art could not make the invention without undue experimentation.

12. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

13. Claims 1 and 2 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

14. Claim 1 is indefinite for using the phrase "at least one of". It has no clearly defined meaning as applied to individual polypeptide. It is therefore not clear what the "at least" features are, nor what else the claimed polypeptide might comprise. Claim 1 is further indefinite as it is not clear where the "60 contiguous residues" is located, such might indicate that the claimed residues is in SEQ ID NO:2, or alternatively might be intended to indicate that the claimed residues is in residues 340-634. Claim 1 is indefinite as it is not clear where the "12 contiguous residues" is located, such might indicate that the claimed residues is in SEQ ID NO:2, or alternatively might be intended to indicate that the claimed residues is in residues 481-634.

A broad range or limitation together with a narrow range or limitation that falls within the broad range or limitation (in the same claim) is considered indefinite, since the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. Note the

explanation given by the Board of Patent Appeals and Interferences in *Ex parte Wu*, 10 USPQ2d 2031, 2033 (Bd. Pat. App. & Inter. 1989), as to where broad language is followed by "such as" and then narrow language. The Board stated that this can render a claim indefinite by raising a question or doubt as to whether the feature introduced by such language is (a) merely exemplary of the remainder of the claim, and therefore not required, or (b) a required feature of the claims. Note also, for example, the decisions of *Ex parte Steigewald*, 131 USPQ 74 (Bd. App. 1961); *Ex parte Hall*, 83 USPQ 38 (Bd. App. 1948); and *Ex parte Hasche*, 86 USPQ 481 (Bd. App. 1949). In the present instance, claim 1 recites the broad recitation at least 60 contiguous residues of SEQ ID NO:2 and at least 12 contiguous residues of SEQ ID NO:2, and the claim also recites residues 340-634 and 481-634 which is the narrower statement of the range/limitation.

Claim 2 recites the limitation "said domain". There is insufficient antecedent basis for this limitation in the claim. Claim 2 also recites the limitation "an sema K1 activity" which is not defined by the claim nor in the art, the specification does not provide a clear definition for ascertaining the term, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. Claim 2 recites the limitation "binding inhibitory activity" which is not defined by the claim, the specification does not provide a clear definition for ascertaining the term, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. The claim 2 is further indefinite for using the phrase "at least one of". It has no clearly defined

meaning as applied to an selected sema K1 activity. It is therefore not clear what the "at least" features are, nor what else the claimed sema K1 activity might comprise. The claim 2 is indefinite for using the phrase "an sema K1-specific immunogenicity". It has no clearly defined meaning as applied to an selected sema K1 activity. It is therefore not clear what the "an sema K1-specific immunogenicity" feature is. The term "antigenicity" in claim 2 is not defined in the art which renders the claim indefinite. The term "antigenicity" is not defined by the claim, the specification does not provide a clear definition for ascertaining the term, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention.

Status of Claims

14. No claims are allowed. All claims stand rejected.

Any inquiry of a general nature or relating to the status of this general application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Papers relating to this application may be submitted to Technology Center 1600, Group 1645 by facsimile transmission. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). Should applicant wish to FAX a response, the current FAX number for Group 1600 is (703) 308-4242.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Li Lee, M.D., Ph.D. whose telephone number is (703) 308-8891. The examiner can normally be reached on Monday-Friday from 8:30 AM to 5:00 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa, can be reached at (703) 308-3995.

Li Lee, M.D., Ph.D.

April 12, 1999

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